CLAIMS

1. A polypeptide (interacting polypeptide) capable of interacting with a Smad polypeptide wherein the interacting polypeptide comprises a Smad Interaction Motif (SIM) and is less than 32 amino acids in length.

2. A polypeptide capable of interacting with a Smad polypeptide wherein the interacting polypeptide comprises the amino acid sequence PP(T/N)K and is less than 32 amino acids in length.

3. A polypeptide comprising the amino acid sequence PP(T/N)K that is less than 32 amino acids in length.

4. A polypeptide capable of interacting with a Smad polypeptide wherein the interacting polypeptide comprises a Smad Interaction Motif (SIM), for example the amino acid sequence PP(T/N)K or three out of four residues thereof, and is not full-length *Xenopus* or human FAST1 or a fragment thereof, mouse FAST2, *Xenopus* Milk, *Xenopus* Mixer, *Xenopus* Bix3 or Bix2.

5. The polypeptide of claim 1 or 4 wherein the SIM comprises at least 8, 9 or 10 of the specified residues (ie not residues designated by an X) of the amino acid sequence D/E-Hyd-$(X)_n$-P-P-(N/T)-K-(T/S)-(I/V)-$(X)_m$-(D/E)-(M/V/I)-$(X)_k$-P

wherein m= 0 to 7; k= 0 to 8 or 12; n = 0 to 15 or 18.

6. The polypeptide of claim 1, 2, 4 or 5 wherein the Smad polypeptide is Smad2 or Smad3.

7. The polypeptide of any one of claims 1 to 6 wherein the polypeptide is a transcription factor or a fragment thereof.

8. The polypeptide of any one of claims 4 to 7 wherein the polypeptide is less than 100 amino acids in length.

9. The polypeptide of any of the preceding claims wherein the polypeptide is between 4 and about 30 or 35 amino acids in length.

10. The polypeptide of any of the preceding claims wherein an acidic amino acid residue is present at a position from 3 to 10 residues C-terminal of the amino acid sequence PP(T/N)K or amino acid sequence corresponding to the PP(T/N)K motif and/or a proline residue is present at a position from 5 to 20 residues C-terminal of the amino acid sequence PP(T/N)K K or amino acid sequence corresponding to the PP(T/N)K motif.

11. The polypeptide of any of the preceding claims comprising the amino acid sequence PPNKTITPDMNVRIPPI or PPNKTITPDMNTIIPQI or PPNKSVFDVLTSHPGD or PPNKSIYDVWVSHPRD or PPNKSIYDVWVSHPRD or PPNKTVFDIPVYTGHPG or PPNKTITPDMNTIIPQI or PPNKTIGPEMKVVIPPL or PPNKSSKRGNTPPW or LLMDFNNFPPNKTITPDMNVRIPPI or HSNLMMDFPPNKTITPDMNTIIPQI or LDNMLRAMPPNKSVFDVLTSHPGD or LDSLFQGVPPNKSIYDVWVSHPRD or LDALFQGVPPNKSIYDVWVSHPRD or

LKNAPSDFPPNKTVFDIPVYTGHPG or HSNLVMEFPPNKTITPDMNTIIPQI or LVEYDNFPPNKTIGPEMKVVIPPL or ITSDAYSDSCPPPNKSSKRGNTPPW.

12. A polypeptide consisting of the amino acid sequence PPNKTITPDMNVRIPPI or PPNKTITPDMNTIIPQI or PPNKSVFDVLTSHPGD or PPNKSIYDVWVSHPRD or PPNKSIYDVWVSHPRD or PPNKTVFDIPVYTGHPG or PPNKTITPDMNTIIPQI or PPNKTIGPEMKVVIPPL or PPNKSSKRGNTPPW or LLMDFNNFPPNKTITPDMNVRIPPI or HSNLMMDFPPNKTITPDMNTIIPQI or LDNMLRAMPPNKSVFDVLTSHPGD or LDSLFQGVPPNKSIYDVWVSHPRD or LDALFQGVPPNKSIYDVWVSHPRD or LKNAPSDFPPNKTVFDIPVYTGHPG or HSNLVMEFPPNKTITPDMNTIIPQI or LVEYDNFPPNKTIGPEMKVVIPPL or ITSDAYSDSCPPPNKSSKRGNTPPW.

13. The polypeptide of any of the preceding claims comprising the amino acid sequence of residues 283 to 307 of Mixer.

14. The polypeptide of any of the preceding claims wherein the said polypeptide is a peptidomimetic compound.

15. A molecule comprising a polypeptide as defined in any of Claims 1 to 14 and a further portion, wherein the said molecule is not full-length *Xenopus* or human

FAST1 or a fragment thereof, mouse FAST2, *Xenopus* Milk, *Xenopus* Mixer or *Xenopus* Bix2.

16. A molecule according to claim 15 wherein the molecule is Biotin.Aminohexanoicacid-
RQIKIWFQNRRMKWKKLLMDFNNFPPNKTITPDMNVRIPPI
or
5-FAM-AMINOHEXANOICACID-
RQIKIWFQNRRMKWKKPEVKNAPKDFPPNKTVFDIPVYTGHPGFLA

17. A nucleic acid encoding or capable of expressing a polypeptide or molecule according to any one of claims 1 to 16.

18. A nucleic acid complementary to a nucleic acid encoding a polypeptide according to any one of claims 1 to 13.

19. An antibody capable of reacting with a polypeptide according to any one of claims 1 to 14.

20. A method of identifying a polypeptide that is capable of interacting with a Smad polypeptide, comprising examining the sequence of a polypeptide and determining that the polypeptide comprises a Smad Interaction Motif (SIM), for example the amino acid sequence PP(T/N)K or three out of four residues thereof.

21. The method of claim 20 comprising determining that the polypeptide comprises at least 8, 9 or 10 of the specified residues (ie not residues designated

by an X) of the amino acid sequence D/E-Hyd-$(X)_n$-P-P-(N/T)-K-(T/S)-(I/V)-$(X)_m$-(D/E)-(M/V/I)-$(X)_k$-P

wherein m= 0 to 7; k= 0 to 8 or 12; n = 0 to 15 or 18.

22. The method of claim 20 or 21 comprising determining that the polypeptide comprises the amino acid sequence PP(T/N)K.

23. The method of claim 20, 21 or 22 further comprising determining that an acid amino acid residue is present at a position from 3 to 10 residues C-terminal of the amino acid sequence PP(T/N)K or amino acid sequence corresponding to the PP(T/N)K motif, and/or a proline residue is present at a position from 5 to 20 residues C-terminal of the amino acid sequence PP(T/N)K or amino acid sequence corresponding to the PP(T/N)K motif.

24. A method of identifying a compound capable of disrupting or preventing the interaction between a Smad polypeptide and a target polypeptide that is (1) a transcription factor capable of interacting with the said Smad polypeptide and/or (2) a polypeptide capable of interacting with the said Smad polypeptide, the interaction requiring α-helix2 of the said Smad polypeptide or (3) a polypeptide comprising the amino acid sequence PP(T/N)K, the method comprising measuring the ability of the compound to disrupt or prevent the interaction between the Smad polypeptide and a polypeptide or molecule according to any one of claims 1 to 16.

25. A compound identified by or identifiable by the method of claim 24 or claim 47.

26. A kit of parts comprising a Smad polypeptide and a polypeptide or molecule according to any one of claims 1 to 16.

27. A method of disrupting or preventing the interaction between a Smad polypeptide and a target polypeptide that is (1) a transcription factor capable of interacting with the said Smad polypeptide and/or (2) a polypeptide capable of interacting with the said Smad polypeptide, the interaction requiring α-helix2 of the said Smad polypeptide, the method comprising exposing the Smad polypeptide to a polypeptide or molecule according to any one of claims 1 to 16 or to an antibody according to claim 19 or to a compound according to claim 25.

28. A method of disrupting or preventing the interaction between a Smad polypeptide and a polypeptide comprising the amino acid sequence PP(T/N)K wherein the Smad polypeptide is exposed to a polypeptide or molecule according to any one of claims 1 to 16 or to an antibody according to claim 19 or to a compound according to claim 25.

29. The method of claim 27 or 28 wherein the Smad polypeptide is Smad2 or Smad3.

30. A compound according to claim 25 or polypeptide or molecule according to any one of claims 1 to 16 or nucleic acid according to claim 17 or 18 or antibody according to claim 19 for use in medicine.

31. A method of modulating activin or TGFβ signalling in a cell *in vitro* wherein the cell is exposed to a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30.

32. A method of modulating activin or TGFβ signalling in a cell *in vivo* wherein the cell is exposed is exposed to a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30.

33. The method of claim 31 or 32 wherein the cell is a late stage tumour cell.

34. The use of a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30 in the manufacture of a medicament for treatment of a patient in need of modulation of activin or TGFβ signalling.

35. The use of a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30 in the manufacture of a medicament for treatment of a patient with cancer.

36. The use of a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30 in the manufacture of a medicament for treatment of a patient in need of reducing extracellular matrix deposition, encouraging tissue repair and/or regeneration, tissue remodelling or healing of a wound, injury or surgery, or reducing scar tissue formation arising from injury to the brain.

37. The use of a polypeptide, molecule, compound, nucleic acid or antibody as defined in claim 30 in the manufacture of a medicament for treatment of a patient with or at risk of end-stage organ failure, pathologic extracellular matrix accumulation, a fibrotic condition, disease states associated with immunosuppression (such as different forms of malignancy, chronic degenerative diseases, and AIDS), diabetic nephropathy, tumour growth, kidney damage (for

example obstructive neuropathy, IgA nephropathy or non-inflammatory renal disease) or renal fibrosis.

38. A method of treating a patient in need of modulation of activin or TGFβ signalling, the method comprising administering to the patient an effective amount of a polypeptide, molecule, compound, nucleic acid or antibody as defined in Claim 30.

39. A method of treating a patient with cancer the method comprising administering to the patient an effective amount of a polypeptide, molecule, compound, nucleic aid or antibody as defined in Claim 30.

40. A method of reducing extracellular matrix deposition or encouraging tissue repair and/or regeneration, or tissue remodelling or healing of a wound, injury or surgery, or reducing scar tissue formation arising from injury to the brain, the method comprising administering for the patient an effective amount of a polypeptide, molecule, compound, nucleic acid or antibody as defined in Claim 30.

41. A method of treating a disease or condition as defined in Claim 37, the method comprising administering to the patient an effective amount of a polypeptide, molecule, compound, nucleic acid or antibody as defined in Claim 30.

42. A substantially pure complex comprising (1) a Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide.

43. A preparation comprising (1) Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide (in the form of a complex or otherwise) when combined with other components *ex vivo*, said other components not being all of the components found in the cell in which said (1) Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide (in the form of a complex or otherwise) are naturally found.

44. A cell comprising 1) a recombinant polynucleotide suitable for expressing a transcription factor that is capable of interacting with a Smad polypeptide and 2) a recombinant polynucleotide comprising a reporter gene driven by a promoter with a binding site for the said transcription factor.

45. A stable cell line cell comprising a reporter gene driven by a promoter with one or more binding sites for an activated Smad, wherein the Smad is activated in the cell by exposure of the cell to TGFβ.

46. The cell according to claim 44 or 45 wherein the reporter gene expresses luciferase, secreted alkaline phosphatase (SEAP), CAT or a green fluorescent protein (GFP).

47. A method of identifying a compound capable of modulating TGFβ-dependent transcription wherein the effect of the compound on expression of the reporter gene in a cell according to claim 44, 45 or 46 is measured, following treatment of the cell with TGFβ.

48. A method of identifying a compound capable of modulating TGFβ-dependent transcription wherein the effect of the compound on TGFβ-signalling-dependent invasive behaviour of a stably-transformed cell line cell, for example in collagen gels, is measured and a compound that reduces invasive behaviour is selected.

49. The method of claim 48 wherein the stably-transformed cell line is a MDCK cell line that is capable of expressing recombinant active Raf-1.